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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/615,865	07/10/2003	Eliezer Konfino	1662/466073	8419

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EXAMINER
KRASS, FREDERICK F

ART UNIT	PAPER NUMBER
1614	

DATE MAILED: 06/01/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/615,865	KONFINO ET AL.	
	Examiner	Art Unit	
	Frederick F. Krass	1614	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *07 April 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *20-32* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *20-32* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *4-7-04*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

Drawings

Insofar as the examiner can determine, no copy of Figures 1 and 2 is present in the IFW application. Applicant is requested to resubmit same.

Written Description ("New Matter") Rejection

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 20-32 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

This is a "new matter" rejection.

1) The specification as originally filed does not describe, implicitly or explicitly, compositions comprising a mixture of polypeptides composed of glutamic acid, lysine, alanine and tyrosine, wherein the mixture of polypeptides is non-uniform with respect to

"constitution", as recited in claim 20. (See the detailed discussion in the related rejection at subsection "1)" of the "Indefiniteness" section hereinunder).

2) Where the PTO has sufficient reason to doubt that a broader described range pertains to the same invention than a narrower (and subsumed) claimed range, then the broader range does not describe the narrower range. In re Wertheim, 541 F.2d 257, 264-265 (CCPA 1976). (Holding that, in light of the description of the invention as employing as employing a solids content in the range of 25-65%, along with specific embodiments of 36% and 50%, the PTO would not have such reason to doubt since persons skilled in the art would consider processes employing a range of 35-60% to be part of the claimed invention). Merely amending claims to conform to values disclosed by the prior art without any originally disclosed basis for narrowing applicant's disclosed range, however, provides sufficient reason to doubt that the originally disclosed broader range does not described the newly claimed narrower range. In re Baird, 348 F.2d 974, 982 (CCPA 1965).

Accordingly, no support is seen in the specification as originally filed for claiming the specific range "about 4 to about 9 kilodaltons" in claim 20, and "about 5 to about 9 kilodaltons" in claim 26. Similarly, no support is seen for the specific recitation of a molecular weight "substantially as depicted in the curves of Figure 1 or Figure 2 in which the average molecular weight is about 7.7 kDa."

Scope of Enablement Rejection

Claims 20-32 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the use of Copolymer-1, does not reasonably provide enablement for using polypeptides "composed of glutamic acid, lysine, alanine and tyrosine". The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

Attention is directed to In re Wands, 8 USPQ2d 1400 (CAFC 1988) at 1404 where the court set forth the eight factors to consider when assessing if a disclosure would have required undue experimentation. Citing Ex parte Forman, 230 USPQ 546 (BdApls 1986) at 547 the court recited eight factors:

1) the quantity of experimentation necessary,
2) the amount of direction or guidance provided,
3) the presence or absence of working examples,
4) the nature of the invention,
5) the state of the prior art,
6) the relative skill of those in the art,
7) the predictability of the art, and
8) the breadth of the claims.

The instant specification fails to provide guidance that would allow the skilled artisan to practice the instant invention without resorting to undue experimentation, as discussed in the subsections set forth hereinbelow.

1. The nature of the invention, state of the prior art, relative skill of those in the art, and the predictability of the art

The invention relates to certain "COP-1" polypeptides, well-known in the art. The relative skill of those in the art is high, generally that of a PHD or MD. This high level of skill, however, is outweighed by the recognized unpredictability of the art.

As is well-known, Copolymer-1 ("COP-1") is a synthetic polypeptide analog of myelin basic protein, having the biological activity of treating multiple sclerosis. It is a complex mixture of polypeptides made by polymerizing alanine, glutamic acid, lysine and tyrosine in a molar ratio of approximately 6:2:5:1, to form products having an average molecular weight of 23,000 daltons. See the instant specification at page 1, lines 8-10, and at the passage spanning page 1, line 32 to page 2, line 4. Such polymerization results in an extremely complex mixture of products, varying both in molecular weight and amino acid sequence. It is unknown, however, which particular product or products within the mixture is responsible for its biological activity. The incorporation of other amino acids likewise has an unpredictable effect on biological activity. See European Patent Application 0 383 620 A2 at page 2, lines 17-30.

2. The breadth of the claims

The rejected claims are extremely broad and inclusive of all polypeptides of alanine, glutamic acid, lysine and tyrosine having a molecular weight between 5 and 9

kilodaltons, irrespective of the relative molar proportions of each amino acid. The claims are also permit the inclusion of other amino acids.

3. The amount of direction or guidance provided and the presence or absence of working examples

The specification provides no guidance for preparing mixtures of polypeptides of alanine, glutamic acid, lysine and tyrosine having the requisite biological activity of treating multiple sclerosis, other than COP-1 (the only species used in the working examples).

4. The quantity of experimentation necessary

Applicant fails to provide information allowing the skilled artisan to ascertain which particular polypeptides comprising alanine, glutamic acid, lysine and tyrosine, other than COP-1 (i.e. the polymerization product of only those four amino acids in the molar ratio of approximately 6:2:5:1) can be used in the instant invention, i.e. to carry out the disclosed utility of the claimed invention, the treatment of multiple sclerosis. The biological activity of such polypeptides is highly unpredictable, and must be determined empirically on a case-by-case basis, with no a priori expectation of success. In the instant case, only one species, COP-1, is exemplified in the working examples. By contrast, the instant claims are very broad and read on polypeptides made from alanine,

glutamic acid, lysine and tyrosine in any relative proportions, and additionally species in which other amino acids could be incorporated. This encompasses an overwhelming number of possible combinations and thus necessitates an exhaustive and undue search for all the embodiments suitable to practice the claimed invention. Given the sheer number of potential combinations of amino acids, and the recognized unpredictability of this art, one would have to mount a massive additional research campaign to determine which combinations within the scope of the instant claims would exhibit the required characteristics. Accordingly, applicant has failed to provide information sufficient to practice the claimed invention absent resorting to undue experimentation.

Indefiniteness Rejection

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 20-32 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

1) The scope of the term "constitution" (claim 20, last line) is entirely unclear. While one can reasonably infer from the specification (as discussed by Applicant in his

preliminary comments) that the instantly claimed polypeptides will vary in molecular weight and amino acid sequence, that is not the same as a mixture's "constitution". That term is essentially subjective in nature; there is no recognized parameter by which a composition's "constitution" can be measured, making it impossible to determine the metes and bounds of the claimed term.

2) Where a claimed value varies with its method of measurement and several alternative methods of measurement are available, the claimed value is indefinite without knowing which method of measurement was used. Honeywell Intl., Inc. v. Intl. Trade Commn., 341 F.3d 1332, 1340 (Fed. Cir. 2003). Accordingly, the term "average molecular weight" (claim 20, second and third lines; claims 24-26; and claim 29) is indefinite since its method of measurement is not specified, i.e. number average molecular weight, weight average molecular weight, average molecular weight as determined by light scattering, etc.

3) Similarly, the percentage values recited in claims 22 and 27 are indefinite without knowing which method was used to compute them, i.e. percent by weight, percent by mole, percent by volume, etc.

4) The term "substantially" in claim 30 is a relative term which renders the claim indefinite. The term "substantially" is not defined by the claim, the specification does not

provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention.

Allowable Subject Matter

Claims 20-32 would be allowable if amended to overcome the outstanding rejections under 35 U.S.C. 112.

The terminal disclaimer submitted by Applicant has been accepted.

The closest prior art of record is European Patent Application 0 383 620 A2, which discloses COP-1 which is produced by recombinant DNA technology. The polypeptides resulting from this process will be uniform in molecular weight and amino acid sequence, and the individual uniform polypeptides can be pooled to form non-uniform mixtures for activity studies. See the first paragraph of page 3. The individual uniform polypeptides may have a lower molecular weight limit of 5 kilodaltons (page 3, line 15), but the prior art provides no direction for pooling such lower molecular weight species to form a non-uniform mixture. Instead, it directs away from same, teaching testing mixtures having much higher molecular weights, on the order of 15-23 kilodaltons. (See page 5, lines 28-34, for example). By contrast, Applicant has factually demonstrated that lower molecular weight Cop-1 has unexpectedly lowered side effects (see pages 5-9 of the instant specification).

Correspondence

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Frederick F. Krass whose telephone number is 571-272-0580. The examiner's schedule is as follows:

Monday: 6:30-3:00PM;
Tuesday: 10-6:30PM;
Wednesday: off;
Thursday: 10-6:30PM; and
Friday: 10-6:30PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Seidel Marianne, can be reached on 571-272-0584. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Frederick Krass
Primary Examiner
Art Unit 1614